Available online at www.sciencedirect.com

ScienceDirect

Procedia IUTAM 12 (2015) 204 – 210

Procedia IUTAM

www.elsevier.com/locate/procedia

IUTAM Symposium on Mechanics of Soft Active Materials

Modeling aneurysm growth and failure

Konstantin Volokh*

Faculty of Civil and Environmental Engineering, Technion – Israel Institute of Technology, Haifa 32000, Israel

Abstract

Aneurysms are abnormal dilatations of vessels in the vascular system. They exist in two major forms: fusiform and saccular. Fusiform aneurysms are found in the human abdominal aorta while saccular aneurysms are found in cerebral blood vessels. The growth and rupture of aneurysms is driven by micro-structural alterations of the vessel, yet precise mechanisms underlying the process remain to be uncovered. Medical treatments of aneurysms are both expensive and dangerous thus a biomechanical approach can be valuable in assisting medical doctors in the process of making decisions.

Biomechanical theories ofaneurysm development should include a description of growth and failure. We argue that the growth description can be done within the framework of continuum mechanics based on the one-to-one mapping of material configurations during the tissue evolution. The latter evolution is accompanied by the alteration of mass density which, in turn, triggers deformations and changes of tissue shape. We also consider a constitutive description of failure based on the concept of energy limiters. The latter means that the strain energy density must be bounded by definition and, thus, the amount of energy that can be stored and dissipated by an infinitesimal material volume must be finite. We discuss some results of the aneurysm simulation based on the described approach.

Peer-review under responsibility of Konstantin Volokh and Mahmood Jabareen.

Keywords: Aneurysm; failure; growth; modeling

1. Introduction

Aneurysms are abnormal dilatations of vessels in the vascular system. They exist in two major forms: fusiform and saccular. Fusiform aneurysms are found in the human abdominal aorta. Saccular aneurysms are found in cerebral blood vessels. The Brain Aneurysm Foundation reports that 2 in 100 people in US have an unruptured brain aneurysm and the annual rate of rupture is about 8-10 per 100,000 people. There is a brain aneurysm rupture every 18 minutes.

* Corresponding author. Tel.: +972-4-8292426; fax: +972-4-8295697.
E-mail address: cvolokh@technion.ac.il

Peer-review under responsibility of Konstantin Volokh and Mahmood Jabareen.
doi:10.1016/j.piutam.2014.12.022

Ruptured brain aneurysms are fatal in about 40% of cases. Of those who survive, about 66% suffer some permanent neurological deficit. Similarly, abdominal aortic aneurysm (AAA) is found in ~2% of the elderly population, with ~150,000 new cases diagnosed each year, and the occurrence is increasing. In many cases AAA gradually expands until rupture causing a mortality rate of 90%. The AAA rupture is considered the 13th most common cause of death in US. Medical doctors consider a surgery option for enlarging AAA, for example, when its maximum diameter reaches 5.5 centimeters or/and expansion rate is greater than 1 cm per year. This simple geometrical criterion may possibly underestimate the risks of rupture of small aneurysms as well as overestimate the risks of rupture of large aneurysms. Biomechanical approaches to modeling aneurysm failure are desired.

Watton et al [1] pioneered mathematical modeling of enlarging aneurysms. Baek et al [2] made another important step in modeling aneurysm growth by introducing a convenient description of evolving strain energy density function. Building on the aforementioned approaches Kroon and Holzapfel [3] developed aneurysm model which was attractive due to its theoretical and computational simplicity. The described works influenced further studies in mathematical modeling of aneurysm growth [4-12]. Though biomechanical features of intracranial and abdominal aortic aneurysms have differences [13], the mathematical grounds of the G&R description can be common in both cases. The mentioned theories were short of a failure description that should be a natural component of the theory. A new paradigm of Growth-Remodeling-Failure (G&R&F) was proposed in [14] by enforcing failure in a description of growth and remodeling. A failure description was enforced with the help of the *energy limiter* constant which provided a saturation value for the strain energy function [15-17]. The energy limiters approach was used in [18] where breakage of individual fibers (or their bonds) was assumed to cause the aneurysm overall rupture.

In the present work we discuss aspects of the mathematical modeling of growth and failure of developing aneurysms in sections 2 and 3 accordingly. In section 4 we discuss the qualitative conclusions regarding aneurysm development and rupture in view of the results of mathematical modeling. It is hoped that these qualitative conclusions can guide future clinical observations and experiments.

2. Growth modeling

The applicability of continuum mechanics to modeling growth of living tissues is not evident in advance. Amusingly, the criticism of the continuum mechanics approach was articulated by Stephen Cowin – the creator of "adaptive elasticity" (the pioneering continuum growth theory) [19]: "The problem is that most continuum models assume smooth bijective mappings of the reference state of an object onto a subsequently deformed state of the same object; bijective means one-to-one and onto. If one examines activities at the cellular level during tissue growth and remodeling the conditions for mappings of this type are not satisfied. Cells move around like guests circulating at a cocktail party, they replicate themselves with some ease and they produce new material for the tissue of which they are a part. If one takes a picture of the reference state of a tissue at the cellular level and then examines a picture of a subsequent state of the tissue one sees regions that were once neighbors now separated by other regions, that there now exist regions that did not exist before and there are regions that existed before that do not exist now. To imagine this, suppose that two jigsaw puzzles were made from the picture of the reference state of a tissue and from the picture of the subsequent state. In a continuum model the puzzle pieces would still fit together in both puzzles but the two puzzles could be different sizes and shapes; the puzzle associated with the deformed state would appear locally as if its picture were stretched like a rubber sheet before the puzzle was cut into pieces. The pieces of the actual cell level puzzles will not be compatible for the two states of the tissue. A piece-by-piece comparison of the cell level puzzle pieces of the two puzzles will uncover missing and additional pieces and pieces that will not fit together. Clearly the real cell level mapping will not be a continuum one-to-one mapping."

Appreciating these thoughts we should note that Stephen Cowin tacitly assumes that *physical particles*, e.g. living cells, and *material points* in continuum mechanics are the same objects. If the assumption is correct then the problem with the use of continuum mechanics for modeling tissue growth is apparent. In our opinion, however, such an assumption is open to criticism. Sharp distinction between the real physical particles and the abstract mathematical concept of a material point should be made. This distinction is illustrated in Fig. 1, in which material deformation-growth is considered on different length scales. On the macroscopic scale, continuum can be divided into an infinite set of material points. It is assumed that position $\mathbf{x}$ in physical space can be ascribed to every material point before growth-deformation. It is further assumed that during growth-deformation every point moves to a new position $\mathbf{y}(\mathbf{x})$ preserving the continuity of the body. This mapping is smooth and bijective. Of course, the concept of the material

point is purely mathematical – it merely refers to very small physical volume. Such small volumes are considered on the mesoscale of the growth-deformation process. It can be seen in Fig. 1 that the material point is a very small physical volume, which in the case of living tissues includes cells, molecules, pores, and various tissue particles. It is crucial to emphasize that the number of material particles does change within the material point due to division and diffusion. Therefore, if the reader could track behavior of a referential material point she would discover a variable mass density within it. The latter means that the referential mass density changes during the deformation-growth and mass is not conserved. This violation of mass conservation is inherent to all open systems exchanging material with their environment.

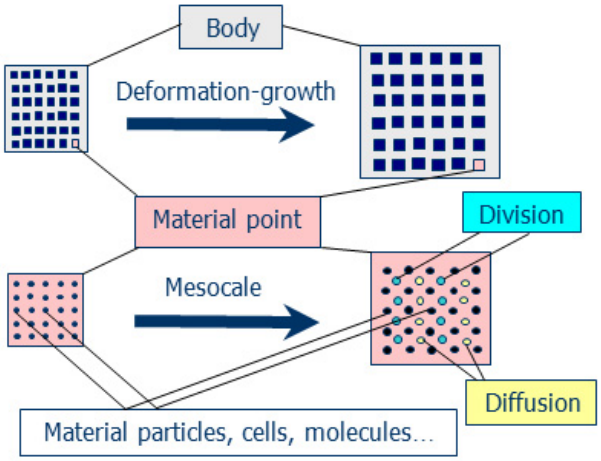

Fig. 1. Multiscale mechanics of growth [20].

Since mass is not conserved – it should obey a general balance law which includes not only volumetric mass supply but also surface mass flux. The latter phenomenon is important for modeling surface growth which is localized in a thin boundary layer [21]. It is interesting, however, that Humphrey and co-authors [2, 22] proposed a way to simplify the growth-deformation coupling by using the integral expression for the evolving strain energy density of a living tissue constituent

$$\psi(t) = \int_{-\infty}^{t} g(t,t_{dp})\dot{m}(t_{dp})f(t,t_{dp})dt_{dp} \tag{1}$$

where $\dot{m}$ is a (dimensionless) rate of the constituent production; f is the strain energy of the deposited constituent; t_{dp} is the time of the constituent deposition; and the life cycle function $g(t,t_{dp})$ is defined by the constituent life time t_{lf} with the help, for example, of the step functions H as follows $g(t,t_{dp}) = H(t-t_{dp}) - H(t-t_{dp}-t_{lf})$.

For example, equation (1) can be reasonably used if the mechanical properties of collagen fibers produced in developing aneurysms do not considerably alter with time. A simple form for the rate of the collagen mass production can be written as follows [3, 18]

$$\dot{m} = \beta \left|\mathbf{M}_{dp}\right|^{2\alpha} \tag{2}$$

where $\mathbf{M}_{dp} = \mathbf{F}(t_{dp})\mathbf{M}$ is a mapping of the unit vector $\mathbf{M}$ in the fiber direction at $t = -\infty$ to the configuration at the time of the collagen fiber deposition $t = t_{dp}$; $\mathbf{F} = \partial \mathbf{y}(\mathbf{x}) / \partial \mathbf{x}$ is the deformation gradient; β and α are constants of material growth.

Unfortunately, the appropriate form of the constitutive equation for the rate of mass supply remains elusive with various authors using various expressions (e.g. [1, 2, 14]). In such a situation the simplest form of the constitutive equation is preferable.

3. Failure modeling

Traditional constitutive models describe deformation but not failure of materials. For instance, the intact behavior of fibers comprising aneurysms can be defined by the following strain energy density function [2, 18]

$$f = \mu(\lambda_{pre}^2 |\mathbf{m}|^2 - 1)^3 \tag{3}$$

where μ is a fiber stiffness parameter; λ_{pre} is a pre-stretch of the deposited fiber; and

$$\mathbf{m} = |\mathbf{M}_{dp}|^{-1} \mathbf{F}_{dp} \mathbf{M}_{dp} = |\mathbf{M}_{dp}|^{-1} \mathbf{F}_{dp} \mathbf{F}(t_{dp})\mathbf{M} = |\mathbf{M}_{dp}|^{-1} \mathbf{F}(t)\mathbf{M} \tag{4}$$

describes the fiber deformation with respect to the time of deposition t_{dp}.

It is important to realize here that deformation of a fiber is measured with respect to configuration at time of the fiber deposition. Indeed, according to (4), the fiber is deposited in the direction of unit vector $\mathbf{M}_{dp} / |\mathbf{M}_{dp}|$ at time t_{dp} and, then, it is mapped into vector $\mathbf{m}$ by the relative deformation gradient $\mathbf{F}_{dp} = \mathbf{F}(t)\mathbf{F}^{-1}(t_{dp})$. An example of inflating idealized axially symmetric membranes made of fiber layers described by constitutive equations (1)-(4) is shown in Fig. 2.

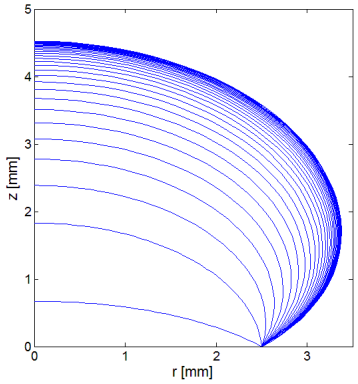

Fig. 2. Evolving shape of the idealized saccular aneurysm [18].

It is noticeable in Fig. 2 that the shape of the evolving aneurysm stabilizes with time and failure is not observed. The failure cannot be observed in principle, of course, because material stays intact according to formula (3). Nevertheless, we do know that aneurysms rupture. This is a result of the onset of material failure from the mechanics standpoint. Thus, to model rupture one should include a description of material failure in the constitutive model. A very simple way to do this is to limit the capacity of material to accumulate and dissipate strain energy [15-17]. The idea of limiting the strain energy density has deep physical roots because it introduces the average energy of molecular bonds in a continuum description of the bulk. To better comprehend the idea let us consider an interaction of two particles. The interaction passes through three stages: repulsion, attraction, and separation. The separation starts at the

limit point of the force-distance curve. The limit point appears due to the existence of the energy limiter – the bond energy – for the particle potential. In the case of tissues composed of billions of particles, the average distance between the particles is measured by strain tensors and the average particle potential is measured by the strain energy function. Amazingly, by analogy with the particle interaction the energy limiter can be introduced in the strain energy functions for continuous media. For example, we can model fiber deformation *and* failure by using the following strain energy density

$$f = 0.1\Phi\{\Gamma[0.1,0] - \Gamma[0.1,(W/\Phi)^{10}]\} \tag{5}$$

$$W = \mu(\lambda_{pre}^2|\mathbf{m}|^2 - 1)^3 \tag{6}$$

where $\Gamma[s,x] = \int_x^\infty t^{s-1}\exp(-t)\,dt$ is the upper incomplete gamma function; Φ is the energy limiter; and W is the strain energy of intact (without failure) material.

Substituting (6) in (5), with account of $|\mathbf{m}| = \lambda$ and $\lambda_{pre} = 1$ for the sake of illustration, and differentiating the latter with respect to stretch it is possible to find the Cauchy stress: $\sigma = \lambda\partial f/\partial\lambda$. The stress-stretch curve is presented graphically in Fig. 3 for $\Phi/\mu = 0.05$. The limit point appears on the graph as a result of the bounded strain energy defined by the limiter, Φ. The limit point corresponds to the onset of failure. It is assumed that fiber rupture is quite abrupt and the post-peak curve goes down steeply. Without the energy limiter the fiber would never break. This is obviously absurd, and physically meaningless.

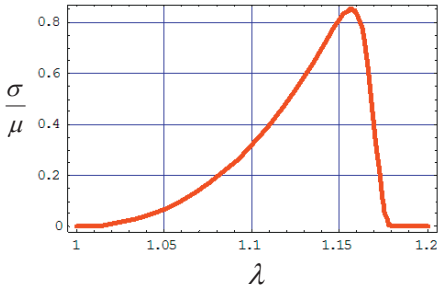

Fig. 3. Sample stress-strain curve for a collagen fiber

Unfortunately, we do not have the experimental data for the uniaxial tension of individual fibers and, thus, computations based on (5)-(6) must include parametric studies. Fortunately, the existing experimental data on the material properties (being controversial) does exhibit some evidence of isotropy of the developed aneurysm. In the latter case it is possible to use a more phenomenological model of the aneurysm deformation and failure, which does not distinguish individual fibers and considers averaged incompressible continuum [14]:

$$f = \Phi\{1 - \exp[-W/\Phi]\} \tag{7}$$

$$W = \alpha_1(\lambda_1^2 + \lambda_2^2 + \lambda_3^2 - 3) + \alpha_2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2 - 3)^2 \tag{8}$$

where λ_i is the principal stretch; and material constants $\alpha_1 = 10.3\,\mathrm{N/cm^2}$; $\alpha_2 = 18.0\,\mathrm{N/cm^2}$; $\Phi = 40.2\,\mathrm{N/cm^2}$ were calibrated in the uniaxial tension test – Fig. 4.

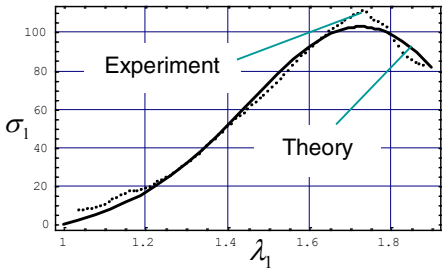

Fig. 4. Cauchy stress [N/cm^2] versus stretch in the uniaxial tension of AAA material [14].

In summary, various descriptions of strain energy functions of the aneurysm material are possible. One can use the micro-structurally guided fiber-based theories or, alternatively, phenomenological macroscopic average theories. It is important, however, that any chosen constitutive theory should incorporate a failure description.

4. Simulations and discussion

The theoretical model of growth, deformation, and failure of collagen fibers described by equations (1)-(6) was used in [18] for simulations of growth and rupture of fusiform and saccular aneurysms. It was assumed that aneurysms were thin axisymmetric membranes comprised of layers of differently oriented collagen fibers. Strength, stiffness, lifetime etc. of the fibers were varied in the finite element simulations of the growth-deformation processes. It was found that for some range of parameters aneurysms stay intact while beyond this range they rupture. Such simple qualitative conclusion is in a good agreement with clinical observations showing that many real aneurysms do not rupture at all. Remarkably, it was found that, according to the obtained numerical results, ruptures occurred very quickly if they occurred at all. The latter theoretical prediction has clinical support. For example, Mitchell and Jakubowski [23] concluded based on statistical analyses that cerebral aneurysms tend to rupture after a short period of intensive growth and those that survive would be much less prone to rupture for a long period. Thus, we conclude that the failure mechanism of the brain aneurysms is related to the rupture of individual collagen fibers whose properties (strength, stiffness, growth constants etc.) do not change throughout the growth process. In other words, the growth-deformation-failure process is so fast that no remodeling happens.

However, another scenario is possible and, probably, takes place for abdominal aortic aneurysms [24-25]. In this case inter-fiber joints fail rather than individual fibers. Mathematically, it means that the energy limiter should be interpreted as an indicator of the inter-fiber joint strength, which should evolve during the aneurysm development (cf. [14]). Physically, it means that the overall aneurysm rupture is caused by disintegration of the fiber net rather than failure of individual fibers. Simulations of the aneurysm growth and failure based on the strain energy density function defined by equations (7)-(8) was considered in [14]. The latter equations were completed with a set of constitutive laws describing material remodeling through the evolution of density, stiffness, and strength. This more sophisticated model predicts ruptures distant in time from the onset of the process of the aneurysm development.

The reader should note that theoretical developments concerning a description of aneurysm growth and rupture have reached a respectable level of sophistication. Unfortunately, experimental calibration of these proposed theories seems beyond reach. The patient-specific prediction of aneurysm rupture based on computer simulations remains a dream. Nevertheless, theoretical studies are not useless. The ones presented in [14] and [18] suggest two different scenarios of the aneurysm development: rupture of individual fibers or disintegration of fiber nets. These scenarios can guide experiments and clinical observations.

References

1. Watton PN, Hill NA, Heil M. A mathematical model for the growth of the abdominal aortic aneurysm. *Biomech. Model. Mechanobiology* 2004; **3**:98–113.
2. Baek S, Rajagopal KR, Humphrey JD. A theoretical model of enlarging intracranial fusiform aneurysms. *J. Biomech. Engng.* 2006; **128**:142-149.
3. Kroon M, Holzapfel GA. A model of saccular cerebral aneurysm growth by collagen fiber remodeling. *J. Theor. Biology* 2007; **247**:775-787.
4. Kroon M, Holzapfel GA. Modeling of saccular aneurysm growth in a human middle cerebral artery. *J. Biomech. Engng.* 2008; **130**:051012.

5. Kroon M, Holzapfel GA. A theoretical model for fibroblast-controlled growth of saccular cerebral aneurysm. *J. Theor. Biology* 2009; **257**:73-83.
6. Chatziprodromou I, Tricoli A, Poulikakos D, Ventikos Y. Hemodynamic and wall remodeling of a growing cerebral aneurysm: A computational model. *J. Biomech.* 2007; **40**: 412-426.
7. Watton PN, Ventikos Y, Holzapfel GA. Modeling the growth and stabilization of cerebral aneurysm. *Math. Medicine Biology* 2009; **26**:133-164.
8. Figueroa CA, Baek S, Taylor CA, Humphrey JD. A computational framework for fluid-solid-growth modeling in cardiovascular simulations. *Comput. Methods Appl. Mech. Engrg.* 2009; **198**:3583-3602.
9. Watton PN, Hill NA. Evolving mechanical properties of a model of abdominal aortic aneurysm. *Biomech. Model. Mechanobiology* 2009; **8**:25–42.
10. Schmid H, Watton PN, Maurer MM, Wimmer J, Winkler P, Wang YK, Rohrle O, Itskov M. Impact of transmural heterogeneities on arterial adaptation: Application to aneurysm formation. *Biomech. Model. Mechanobiology* 2010; **9**:295-315.
11. Martufi G, Gasser TC. Turnover of fibrillar collagen in soft biological tissue with application to the expansion of abdominal aortic aneurysms. *J. R. Soc. Interface* 2012; **9**:3366-3377.
12. McGloughlin T (ed). *Biomechanics and Mechanobiolgy of Aneurysms*. Springer-Verlag; 2011.
13. Humphrey JD, Taylor CA. Intracranial and abdominal aortic aneurysms: similarities, differences, and need for a new class of computational models. *Annu. Rev. Biomed. Eng.* 2008; **10**:221-46.
14. Volokh KY, Vorp DA. A model of growth and rupture of abdominal aortic aneurysm. *J. Biomech.* 2008; **41**:1015-1021.
15. Volokh KY. Modeling failure of soft anisotropic materials with application to arteries. *J. Mech. Behav. Biomed. Materials* 2011; **4**:1582-1594.
16. Volokh KY. Review of the energy limiters approach to modeling failure of rubber. *Rubber Chem. Technology* 2013; **86**:470-487.
17. Volokh KY. On irreversibility and dissipation in hyperelasticity with softening. *J. Appl. Mech.* 2014; **81**:074501.
18. Balakhovsky K, Jabareen M, Volokh KY. Modeling rupture of growing aneurysms. *J. Biomech.* 2014; **43**:653-658.
19. Cowin SC. On the modeling of growth and adaptation. In: *Mechanics of Biological Tissue*. Eds. GA Holzapfel and RW Ogden. Springer; 2005.
20. Volokh KY. Stresses in growing soft tissues. *Acta Biomaterialia* 2006; **2**:493-504.
21. Volokh KY, Lev Y. Growth, anisotropy, and residual stresses in arteries. *Mech. Chem. Biosyst*. 2005; **2**:27-40.
22. Humphrey JD, Rajagopal KR. A constrained mixture model for growth and remodeling of soft tissues. *Math. Models Meth. Appl. Sci.* 2002; **12**:407-430.
23. Mitchell P, Jakubowski J. Estimate of the maximum time interval between formation of cerebral aneurysm and rupture. *J. Neurol. Neurosurg. Psychiatry* 2000; **69**:760-167.
24. Humphrey JD. *Cardiovascular Solid Mechanics: Cells, Tissues, and Organs*. Springer-Verlag; 2002.
25. Sakalihasan N, Limet R, Defawe OD. Abdominal aortic aneurysm. *Lancet* 2005; **365**:1577-1589.